

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 62457

**Title:** Stem cell injection for complex anal fistula in Crohn's disease: Single-center experience focusing on patient selection and long-term outcome

**Reviewer's code:** 00049331

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Professor

**Reviewer's Country/Territory:** Turkey

**Author's Country/Territory:** Germany

**Manuscript submission date:** 2021-01-09

**Reviewer chosen by:** Jin-Lei Wang

**Reviewer accepted review:** 2021-01-11 14:53

**Reviewer performed review:** 2021-01-13 01:01

**Review time:** 1 Day and 10 Hours

<b>Scientific quality</b>	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

In this prospective study, the Authors aimed to evaluate the long-term outcome of local administration of allogenic, adipose-derived mesenchymal stem cells for complex anal fistula associated with Crohn`s disease. This study has been well written, but I have some minor suggestion. Study population: Definition of complex anorectal fistulas should be more ascertain (intersphincteric, trans-sphincteric, suprasphincteric ...). Discussion: One of the limitations of the current study is small patients` collective, and another of that is the absence of the control group. Actually the Authors indicated the limitation and recommended further efforts including controlled studies about that in the conclusion. However both limitations should be mentioned in the discussion section.

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**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 62457

**Title:** Stem cell injection for complex anal fistula in Crohn's disease: Single-center experience focusing on patient selection and long-term outcome

**Reviewer's code:** 00036458

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** France

**Author's Country/Territory:** Germany

**Manuscript submission date:** 2021-01-09

**Reviewer chosen by:** Jin-Lei Wang

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**Reviewer performed review:** 2021-01-15 15:35

**Review time:** 5 Days and 7 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

This is a very interesting article on a very hot topic for Crohn's disease with ano-perineal fistula and a long follow up. I have a few questions and remarks: There is many debates about the criteria for healing; either the Present's criteria and/or MRI criteria. The paragraph in the discussion about the definition of healing should be added into the methods. Table 2 should be added as a paragraph in the method section to be more apparent. Did you do the PDAI score? Recent data showed that fibrin glue injection or other local method are disappointing. One of the predictor of response is the medical treatment. It is suprizing that no patient had a combinaison of anti-TNF and immunomodulators. How do you explain this? How many patients had their medical treatment change after the stem cell treatment? Patients with major medical changes after injection should not be considered in remission thanks to the stem cell treatment. In addition, patients with abscess should not be considered in remission even a long time after injection. Did they have MRI to diagnose a fistula? Or did they have medical change for the Crohn's disease because of the abcess? I do not think that figure 1 and 2 bring important information. The discussion is too long. You could shorten the paragraph about the COVID as we understand the higher difficulties to perform a protocol during this period.

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**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 62457

**Title:** Stem cell injection for complex anal fistula in Crohn's disease: Single-center experience focusing on patient selection and long-term outcome

**Reviewer's code:** 03812467

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Research Fellow

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Germany

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**Reviewer chosen by:** AI Technique

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**Review time:** 7 Days and 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

#### **SPECIFIC COMMENTS TO AUTHORS**

The application of adipose-derived mesenchymal stem cells (Darvastrocel) to study the therapeutic effect of patients with perianal fistula Crohn's disease is a very innovative and practical study. The only limitation is that the number of case specimens is small, and we look forward to further progress in the future for the multi-sample and multi-center clinical research.